

## Research Article

# Comparison of optic disc images from two smartphone-based imaging systems in glaucoma patients and suspects

Nattapon Boonarpa, PhD<sup>1,2</sup>, Paul C Knox, PhD<sup>1,2</sup>, Mark Batterbury, FRCOphth<sup>1,2</sup>, Clare Rogers, FRCOphth<sup>1,2</sup> and Yalin Zheng, PhD<sup>1,2</sup>

<sup>1</sup>Department of Eye and Vision Science, University of Liverpool, Liverpool, United Kingdom

<sup>2</sup>St. Paul's Eye Unit, The Royal Liverpool University Hospital, Liverpool, United Kingdom

## Abstract

**Purpose:** To compare the quality of retinal images obtained with the iExaminer system and D-Eye with those of a standard digital retinal camera.

**Methods:** We conducted a prospective observational study on patients with confirmed or suspected glaucoma. Images from both undilated and dilated eyes of all patients were acquired by both smartphone devices (iExaminer system and D-Eye) while a single image was acquired using Kowa 3D fundus camera (dilated). All images were acquired by the same trained operator. All the acquired images were cropped and normalised to the same size followed by grading on the image quality and cup-disc ratio by two masked graders. Statistical analysis was performed with SPSS v22 (SPSS Inc., IBM, USA).

**Results:** 103 patients (39 diagnosed glaucoma, 37.9%) were recruited, providing a dataset of 515 optic disc images. The proportions of images suitable for cup and disc measurements obtained from dilated eyes by D-Eye and iExaminer were statistically significantly lower when compared to that of the Kowa camera ( $P < 0.05$ ). For images graded as at least acceptable, inter-observer agreement for the cup-to-disc ratio extracted from them was good with intraclass correlations (ICCs) of 0.885 or better, with no marked differences between devices, and no great improvement with dilation. Intra-observer agreement was also good (ICC = 0.909 or better) across devices and conditions.

**Conclusion:** Smartphone-based imaging approaches showed encouraging results in imaging the optic disc of patients with diagnosed or suspected glaucoma. Further development is needed to make them usable to aid management of eye disease.

**Correspondence to:** Dr. Yalin Zheng, Department of Eye and Vision Science, University of Liverpool, Liverpool, L7 8TX, United Kingdom, Tel: +44 (0)151 794 9055; E-mail: yalin.zheng@liverpool.ac.uk

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## Introduction

High quality imaging of ocular structures plays an important role in ophthalmology. Photographs of the posterior segment, capturing images of structures such as the macula, optic disc and retinal vessels are important in screening for disease, and for the diagnosis and monitoring of a number of critical conditions such as diabetic retinopathy and glaucoma. Once obtained, images must also be recorded, assessed or analysed and archived. However, standard desktop fundus cameras are relatively expensive items of equipment, usually operated by skilled technicians. It is not surprising therefore that attention has turned to whether the near ubiquitous smartphone might be able to provide usable images of eye structures<sup>1,2</sup>. As smartphone camera technology has improved rapidly in recent years (along with their computing power and inherent connectivity), they have evolved from being used as an addition to standard equipment such as a slit lamp or ophthalmoscope; specialised attachments and apps have been developed to allow their use as an independent imaging modality<sup>3-5</sup>. With a number of these attachments moving from the prototype stage to commercial availability, there is a need to assess the clinical utility of smartphone-based imaging approaches.

Retinal imaging, particularly of the optic disc, is important in the diagnosis and monitoring of glaucoma<sup>6</sup>. Over an extended period there has been considerable discussion of the relative merits of various disc and optic cup measurements<sup>7-11</sup>. Other features that might be extracted from photographs of optic discs, such as blood vessel width around the disc margin, have also been suggested to have diagnostic value<sup>12</sup>. Therefore imaging of the disc and the extraction of relevant parameters provides a clinically meaningful context for the evaluation of smartphone-based retinal imaging systems. Indeed recent studies have compared optic disc

images obtained with a prototype smartphone device to a standard digital retinal camera system<sup>13</sup>, and between a smartphone device and slit-lamp biomicroscopy for grading the vertical cup-to-disc ratio<sup>14</sup>.

We undertook a comparative study of two commercially available smartphone-based systems. One, the D-Eye, is a small smartphone attachment, which allows coaxial illumination of the eye, and depends primarily on the optics of the smartphone camera. The second system, the iExaminer, provides a means of securely attaching an iPhone to an ophthalmoscope in order to capture images. We used these devices to obtain optic disc images from both undilated and dilated eyes in glaucoma suspects and glaucoma patients attending a routine outpatient clinic. Smartphone images were compared with images obtained on a standard digital retinal camera.

## Materials and methods

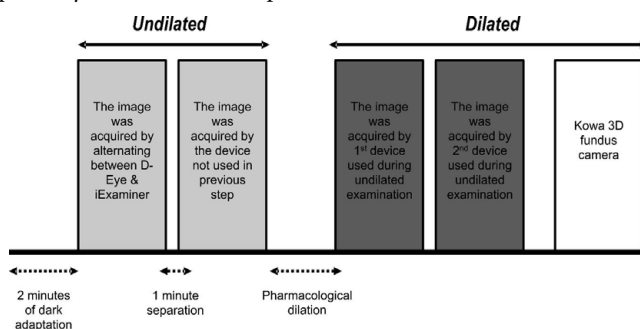
### Participants

We conducted a prospective observational study on patients with confirmed or suspected glaucoma, aged between 18 and 80 years, who were attending the South Liverpool NHS Treatment Centre for a scheduled monitoring visit. Patients were excluded if they were unable to provide informed consent, could not cooperate with the required tests or had ocular media opacities, such as a dense cataract, which might preclude obtaining clear images of the optic disc.

The study was fully explained to each potential patient before obtaining written informed consent. The study was approved by the UK HRA/NRES Research Ethics Committee North West (15/NW/0653) and undertaken in accordance with the tenets of the Declaration of Helsinki.

### Clinical setting

One randomly selected eye per patient was assigned as an index eye. All patients underwent an examination of the optic disc using three ophthalmic imaging devices: two smartphone-based devices (iExaminer system, Welch Allyn, Skaneateles Falls, NY; D-Eye, D-Eye Srl, Padova, Italy) and one reference desktop retinal imaging camera (Kowa 3D fundus camera, Kowa Optimed Inc, Tokyo, Japan). The order of smartphone devices used to capture the optic disc was randomly assigned for each patient and the same order was applied to obtain images from both undilated and dilated eyes. For undilated eyes, imaging was preceded by a 2-minute dark adaptation period, and there was a 1-minute recovery period between each device (Figure 1). After the completion of undilated photography, the pupil was pharmacologically dilated with tropicamide 1%. The same smartphone imaging sequence was then used for dilated eyes. Finally, a photograph was acquired using the Kowa 3D fundus camera. Thus a total of 5 images of the optic disc were acquired from each patient. All photographs were acquired by the same trained operator (author NB).



**Figure 1:** The sequence of the optic disc photography taken from each patient.

## Devices and procedures

### D-Eye

The D-Eye (Figure 2A) consisted of an iPhone 5 (Apple Inc, Cupertino, California, USA) with an image resolution of  $3264 \times 2448$  pixels and the D-Eye adapter (described in detail in <sup>15</sup>) which is magnetically attached to the iPhone. To avoid touching patient's nose, the iPhone was held vertically for the right eye and horizontally for the left eye. The distance between the D-Eye adapter and the patient's eye was approximately 1 – 3 cm. The image of the optic disc was captured in accordance with the device manual. For emmetropic eyes the D-Eye was focused on an object at a distance of 3m. When the object was in focus, the auto-focus mode was locked before attempting to capture disc images.

For myopic eyes (refractive error  $\leq -2D$ ) and hyperopic eyes (refractive error  $\geq +2D$ ), the focus was adjusted and locked according to the patient's refraction using a distance guideline provided in the manual. First, a 30 second video with standard quality was obtained, followed by images in the 20 multiple shot mode in which the iPhone was set to capture a single image of the optic disc continuously every 2 seconds. The best single image of the disc, judged by the operator at the time, was selected for further analysis.

### iExaminer

The iExaminer (Figure 2B) apparatus consists of an iPhone 4s (image resolution of  $3264 \times 2448$  pixels) attached to a panoptic ophthalmoscope via an iExaminer adapter.

The illumination of the ophthalmoscope was set to medium and the large aperture set. The iPhone was set to auto-brightness. To image the right and the left eyes, the operator approached the patient from same side facing the patient. The panoptic ophthalmoscope was held at the level of the patient's eye to image the optic disc. The focus of the panoptic ophthalmoscope was then adjusted to obtain a clear view of the disc. Nine consecutive real time images of the optic disc were captured in 3 seconds with the high resolution capturing mode. The best image displayed on the iPhone screen was selected and saved to the patient's profile. Again, the best quality image, judged by the operator, was selected for further analysis.

### Kowa 3D fundus camera

The reference colour image of the optic disc was captured using Kowa 3D fundus camera. The patient was asked to fixate at the flashing green light while the image was captured. Two parallel images of the optic disc were captured but only the highest image quality judged by the operator was selected for the study.

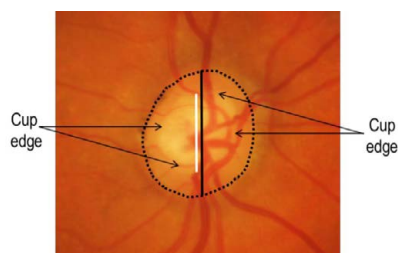


**Figure 2:** Smartphone devices used in this study, D-Eye (A: <https://www.d-eyecare.com>) and iExaminer (B: <https://www.welchallyn.com>)

## Optic disc and optic cup assessments

As the acquired images from different cameras had different fields of view and different image sizes, structures such as the same optic disc (OD) had a range of sizes in different images. In order to make each OD similar, to remove size cues for grading, images were cropped and resized prior to grading. More specifically, an area centred on the OD with an estimated width and height of 2 OD diameters was cropped from each image, which was then resized to  $800 \times 800$  pixels. All the cropped images were saved as TIF format in order to avoid loss of quality. This was done by the same operator (author NB) using a customised program written in Matlab R2016a 64-bit (The Mathworks, Natick, MA, USA). During grading, the cropped images were displayed on a large computer screen calibrated for the grading of retinal images at the Liverpool Reading Centre.

Two masked graders (author NB and an independent experienced ophthalmic grader from the Liverpool Reading Centre) graded all the images independently, following a study specific grading protocol adapted from the NICOLA Study (Network UK. NICOLA Study – Supplement 4. 2015). Images were presented in random order, with patient identifying information, disease status and camera information removed. The optic disc and optic cup are defined as the outer and the inner border of the neuroretinal rim, respectively (Figure 3). For all images, the image quality of the optic disc was categorized as 0 (inadequate; <50% disc edge can be seen), 1 (adequate; >50% and <90% disc edge can be seen) to 2 (good; >90% disc edge can be seen). The quality of the optic cup was categorised in terms of visibility of the cup edge (instead of the disc edge for the disc grading). Optic disc or optic cup (OC) of quality score 1 or 2 are deemed as gradeable. Then the heights of the OD and OC were assessed as measurable or not based on whether the grader was >90% confident that they could be measured. The OD height is the vertical distance from the superior to inferior outer border of the rim while the cup height is the vertical distance from the superior to inferior inner border of the rim. For measurable images, the heights of the OD and the OC were measured by the same grader at the same time using the in-house program. The OD and OC height values were used to calculate the cup to disc ratio (CDR; Figure 3) only when both of the measurements were available. In addition, in order to establish the intra-observer agreement, one grader (author NB) repeated the grading and measurement tasks one week after the first grading masked from the results of the first round.



**Figure 3:** Main features used for optic disc assessment including the disc edge defined as the outer border of the neuroretinal rim (dotted line) and the cup edge defined as the inner border of the neuroretinal rim (arrows). The vertical distances of the cup (white line) and the disc (black line) were measured and used to calculate the cup to disc ratio (CDR).

## Statistical methods

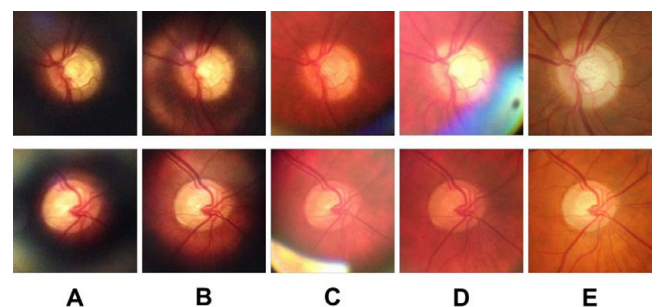
Statistical analysis was performed with SPSS v22 (SPSS Inc., IBM, USA). McNemar's test was used to determine the difference in the proportions of images suitable for OC/OD measurements between the smartphone-based devices and the reference. Inter- and intra-

observer agreement on grading were evaluated using Cohen's kappa coefficient  $\kappa$  ( $\kappa < 0.20$  signifies poor agreement,  $\kappa = 0.21 - 0.40$  signifies fair agreement,  $\kappa = 0.41 - 0.60$  signifies moderate agreement,  $\kappa = 0.61 - 0.80$  signifies substantial agreement and  $\kappa = 0.81 - 1.00$  signifies almost perfect agreement<sup>16</sup>). The reliability of the CDR measurements was assessed using the intraclass correlation coefficient (ICC) and Bland-Altman analysis<sup>17</sup>. A P-value of 0.05 was considered statistically significant.

## Results

We successfully obtained images for grading from 103 patients, providing a dataset of 515 images. Thirty-nine patients had a glaucoma diagnosis (37.9%) and 64 patients (62.1%) were glaucoma suspects. The mean age of all patients was 66.2 years (95% confidence interval [CI], 63.6 – 68.8 years). The mean pupil diameter was 3.0 (95% CI 2.9 – 3.1) mm before and 6.9 (95% CI 6.7 – 7.1) mm after pharmacological dilatation. No adverse effects were observed following the image acquisition using either D-Eye or iExaminer. The average time taken to capture images from undilated eyes was 147.6s (95%CI, 132.5 - 162.7s) for the iExaminer and 160.7s (95% CI, 151.5 - 169.9s) for the D-Eye. Although the time taken by iExaminer was statistically significantly shorter than D-Eye ( $P = 0.011$ , Wilcoxon Signed Ranks test), the D-Eye was used to obtain both single and video images. On average it takes about 30s to acquire a video.

Representative cropped and resized images obtained from two patients (one with glaucoma, one a glaucoma suspect) using the different devices are shown in Figure 4.



**Figure 4:** Representative cropped and resized images from a glaucoma patient (TOP) and a glaucoma suspect (BOTTOM), (A) D-Eye with undilated pupil, (B) D-Eye with dilated pupil, (C) iExaminer with undilated pupil, (D) iExaminer with dilated pupil and (E) KOWA 3D fundus camera (dilated).

## Proportions of images suitable for OC/OD measurements

Example images graded as suitable for OC/OD measurement by each grader (Grader 1 and Grader 2, 1<sup>st</sup> grading) are shown in Figure 4. The number of images deemed to have adequate and/or above quality by both graders were: 70 images by Kowa with dilation, 32 by D-Eye without dilation, 40 by D-Eye with dilation, 15 by iExaminer without dilation, and 22 using iExaminer with dilation. For images acquired using KOWA-3D fundus camera, 77% and 78% were graded as suitable for further analysis (note that these images were only obtained from dilated eyes). The proportions of images suitable for OC/OD measurements obtained from dilated eyes by D-Eye and iExaminer were statistically significantly lower when compared to that of the KOWA camera ( $P < 0.05$ , McNemar's Test) and the agreement between graders more variable. The proportions were generally higher with dilation for the same grader for both the D-Eye and the iExaminer. For the D-Eye the difference was not statistically significant. For the

iExaminer (undilated G1:17%/G2:24%; dilated G1:31%/G2:38%) the difference was statistically significant ( $P < 0.05$ , McNemar's Test). The proportions were consistently higher for the D-Eye compared to the iExaminer. Although grader 2 consistently identified more gradable images than grade 1, the ranking of the proportions of gradable images of different devices with and without dilation remains the same.

**Table 1:** The proportions of images graded as having quality for measuring optic disc and optic cup parameters.

	Grader 1	Grader 2 (1 <sup>st</sup> grade)
Device	Measurable OC/OD	Measurable OC/OD
<b>KOWA</b>	77 (75%)	78 (76%)
<b>Undilated D-Eye*</b>	44 (43%)	59 (57%)
<b>Dilated D-Eye*</b>	47 (46%)	67 (65%)
<b>Undilated iExaminer*†‡</b>	18 (17%)	25 (24%)
<b>Dilated iExaminer*†‡±</b>	32 (31%)	39 (38%)

McNemar's Test; \*,  $P < 0.05$  compared to KOWA; †,  $P < 0.05$  compared to undilated D-Eye; ‡,  $P < 0.05$  compared to dilated D-Eye and ±,  $P < 0.05$  compared to undilated iExaminer

### Inter-observer, intra-observer, inter-method agreements

The inter- and intra-observer agreement on grading are shown in Table 2. More specifically, when we compared the agreement on the proportion of images graded as suitable for OC/OD measurement from each device between graders (G1 vs G2, 1<sup>st</sup> grading), moderate inter-observer agreement was found in images captured using KOWA 3D fundus camera and iExaminer without pupil dilation. Poor to fair inter-observer agreements were found in images captured using D-Eye with and without pupil dilation and iExaminer with pupil dilation. When we compared the agreement on the proportion of images graded as suitable for OC/OD measurement from each device from the same grader at different sessions (G2 1<sup>st</sup> grading vs G2 2<sup>nd</sup> grading), substantial intra-observer agreement was found in images captured using KOWA 3D fundus camera and both smartphone devices with and without pupil dilation.

**Table 2:** Inter- and intra-observer agreement on image quality grading for each device

Devices	Inter-observer ( $\kappa$ )	Intra-observer ( $\kappa$ )
<b>KOWA</b>	0.609	0.620
<b>Undilated D-Eye</b>	0.258	0.746
<b>Dilated D-Eye</b>	0.357	0.705
<b>Undilated iExaminer</b>	0.621	0.891
<b>Dilated iExaminer</b>	0.423	0.722

$\kappa$ , kappa coefficient

### Reliability of CDR

For the images graded as suitable for OC/OD measurement by both graders, three analyses of the agreement on the CDR values were performed: 1) inter-observer agreement using the CDR values from Grader 1 and 1<sup>st</sup> CDR from Grader 2, 2) intra-observer agreements using the CDR values from 1<sup>st</sup> and 2<sup>nd</sup> CDR values from Grader 2, and 3) the agreements on the CDR values from each smartphone device and the reference standard.

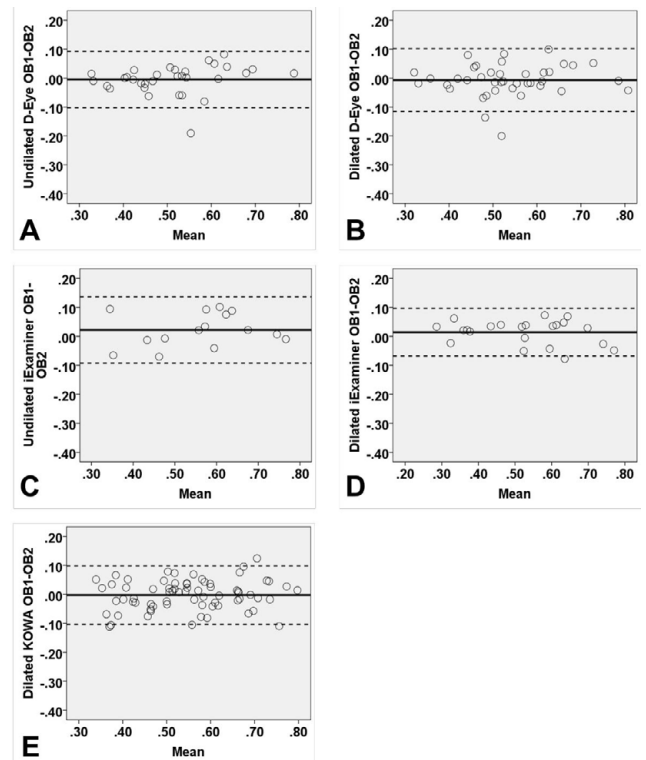
#### Inter-observer agreement on CDRs

The ICC for inter-observer measurement agreement was 0.909 (95% CI, 0.858 – 0.943) for images acquired using KOWA 3D fundus camera. The ICCs were 0.902 (95% CI, 0.810 – 0.951) for images acquired using D-Eye without pupil dilation and 0.885 (95% CI, 0.793 – 0.937) with pupil dilation. The ICCs were 0.894 (95% CI, 0.717 – 0.963) for images acquired using iExaminer without pupil dilation and 0.954 (95% CI,

0.891 – 0.981) with pupil dilation. The mean differences of the CDR values were larger for images acquired using iExaminer compared to D-Eye and KOWA 3D fundus camera as shown in Table 3. Figure 5 shows the Bland-Altman plots for inter-observer measurements of the CDR from each device. An increasing inter-observer bias (the distance between the mean difference and the corresponding zero difference) was observed in images acquired using iExaminer with or without pupil dilation.

**Table 3:** Inter-observer agreement on CDRs.

Devices	N	ICC (95% CI)	Mean difference (95% CI)	95% limits of agreement
<b>KOWA</b>	70	0.909 (0.858 - 0.943)	-0.002 (-0.014 - 0.010)	-0.103 - 0.099
<b>Undilated D-Eye</b>	32	0.902 (0.810 - 0.951)	-0.005 (-0.023 - 0.013)	0.103 - 0.093
<b>Dilated D-Eye</b>	40	0.885 (0.793 - 0.937)	-0.007 (-0.025 - 0.011)	-0.115 - 0.102
<b>Undilated iExaminer</b>	15	0.894 (0.717 - 0.963)	0.022 (-0.010 - 0.054)	-0.092 - 0.136
<b>Dilated iExaminer</b>	22	0.954 (0.891 - 0.981)	0.014 (-0.004 - 0.033)	-0.068 - 0.097



**Figure 5:** Bland-Altman plots showing inter-observer with mean difference (Thick line) and 95% limits of agreement (dashed line) for CDRs by each device, (A) D-Eye without pupil dilation, (B) D-Eye with pupil dilation, (C) iExaminer without pupil dilation, (D) iExaminer with pupil dilation and (E) KOWA 3D fundus camera.

#### Intra-observer agreement on CDRs

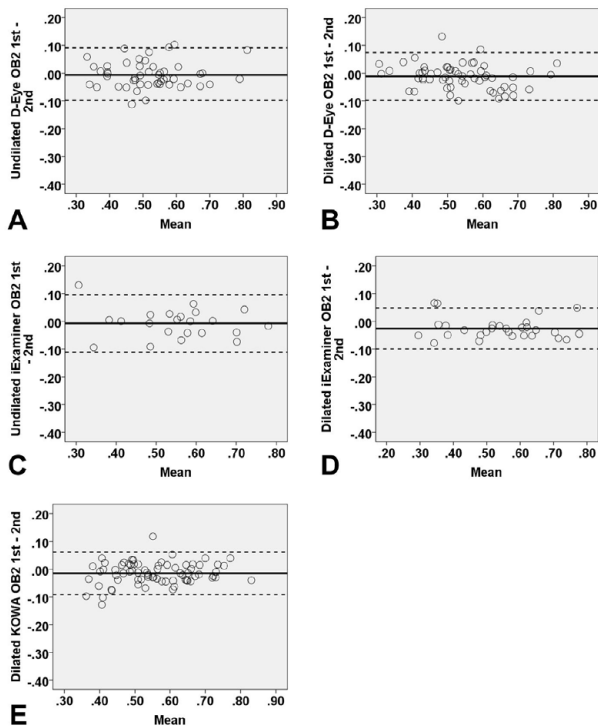
The ICCs for intra-observer measurement agreement was 0.931 (95% CI, 0.880 – 0.959) for images acquired using KOWA 3D fundus camera. The ICCs were 0.909 (95% CI, 0.846 – 0.947) for images acquired using D-Eye without pupil dilation and 0.923 (95% CI, 0.872 – 0.954) with pupil dilation. The ICCs were 0.912 (95% CI, 0.802 – 0.962) for images acquired using iExaminer without pupil dilation and 0.949 (95% CI, 0.825 – 0.981) with pupil dilation. The mean differences and 95%



limits of agreement on the CDR generated by the same grader are shown in Table 4. Figure 6 shows the Bland-Altman plots for intra-observer measurements of the CDR from each device. Greatest intra-observer bias was observed for images acquired using iExaminer with pupil dilatation.

**Table 4:** Intra-observer agreement on the cup disc ratio measurement.

Devices	N	ICC (95% CI)	Mean difference (95% CI)	95% limits of agreement
<i>KOWA</i>	72	0.931 (0.880 - 0.959)	-0.015 (-0.024 - -0.006)	-0.092 - 0.062
<i>Undilated D-Eye</i>	50	0.909 (0.846 - 0.947)	-0.006 (-0.020 - 0.007)	-0.098 - 0.086
<i>Dilated D-Eye</i>	59	0.923 (0.872 - 0.954)	-0.012 (-0.024 - -0.001)	-0.098 - 0.074
<i>Undilated iExaminer</i>	22	0.912 (0.802 - 0.962)	-0.007 (-0.031 - 0.016)	-0.111 - 0.096
<i>Dilated iExaminer</i>	29	0.949 (0.825 - 0.981)	-0.026 (-0.040 - -0.012)	-0.100 - 0.048



**Figure 6:** Bland-Altman plots showing intra-observer with mean difference (Thick line) and 95% limits of agreement (dashed line) for CDR values by each device, (A) D-Eye without pupil dilation, (B) D-Eye with pupil dilation, (C) iExaminer without pupil dilation, (D) iExaminer with pupil dilation and (E) KOWA 3D fundus camera

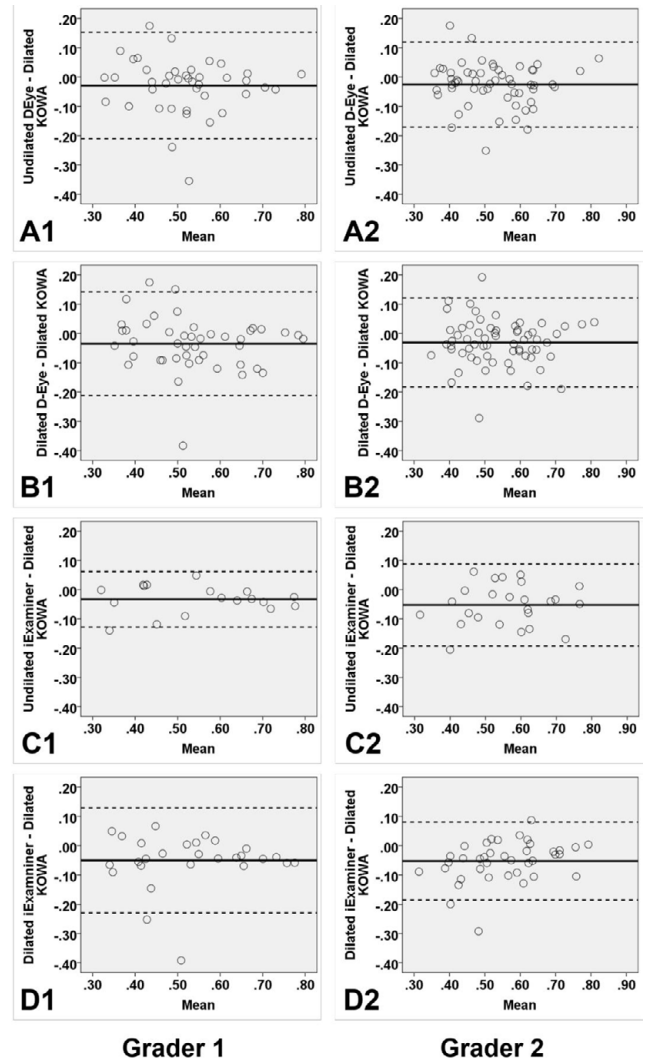
## CDR agreement between smartphone devices and the reference standard

The reliability of the CDR calculated from images obtained with each of the smartphone devices was compared against the reference standard, the KOWA 3D fundus camera, for both graders. The CDR for both smartphone devices was consistently lower than that generated from images obtained using the KOWA camera; these differences were not statistically significant (Table 5). However, the mean differences of the CDR against the reference were significantly larger in images captured using iExaminer compared to that of D-Eye ( $P < 0.05$ ). Figure 7 shows the Bland-Altman plots for the CDR from each device compared to the reference. When the CDR was compared to the reference standard, the tendency of bias increased in images acquired using iExaminer compared to D-Eye for both graders.

**Table 5:** Comparison on the CDR between the smartphone devices and the reference.

Grader	Devices	N	ICC (95% CI)	Mean difference (95% CI)	95% limits of agreement
<i>Grader 1</i>	<i>Undilated D-Eye</i>	41	0.670 (0.458-0.810)	-0.029 (-0.058-0.000)	-0.211-0.153
	<i>Dilated D-Eye</i>	45	0.718 (0.523-0.839)	-0.035 (-0.062-0.008)	-0.212-0.142
	<i>Undilated iExaminer</i>	18*	0.931 (0.744-0.977)	-0.033 (-0.057-0.009)	-0.128-0.062
	<i>Dilated iExaminer</i>	28*	0.741 (0.450-0.880)	-0.050 (-0.086-0.015)	-0.229-0.129
<i>Grader 2</i>	<i>Undilated D-Eye</i>	56	0.772 (0.628-0.863)	-0.026 (-0.045-0.006)	-0.171-0.120
	<i>Dilated D-Eye</i>	64	0.735 (0.569-0.838)	-0.031 (-0.050-0.012)	-0.182-0.120
	<i>Undilated iExaminer</i>	25*	0.769 (0.372-0.908)	-0.052 (-0.082-0.023)	-0.193-0.088
	<i>Dilated iExaminer</i>	39	0.774 (0.380-0.903)	-0.052 (-0.075-0.030)	-0.186-0.081

Wilcoxon Signed Ranks Test; \*,  $P < 0.05$  compared to dilated D-Eye



**Figure 7:** Bland-Altman plots showing the mean difference (Thick line) and 95% limits of agreement (dashed line) for CDR values between each smartphone device and the reference (dilated KOWA), (A) D-Eye without pupil dilation, (B) D-Eye with pupil dilation, (C) iExaminer without pupil dilation and (D) iExaminer with pupil dilation

## Discussion

In this study we compared images of the optic disc obtained with two commercially available smartphone-based imaging systems with those obtained using a standard digital clinical fundus camera as a reference. We graded the images obtained from both undilated and dilated eyes using a standard protocol and then investigated the reliability with which the CDR could be measured from those images graded as at least adequate.

For images obtained from dilated eyes, which could be directly compared between the smartphone devices and the Kowa, while both smartphone devices produced a lower proportion of images graded as suitable for further analysis, the D-Eye produced a consistently higher proportion compared to the iExaminer. However, it should be noted that inter-observer agreement was lower for the D-Eye. The two graders that were involved in the evaluation of the images were both trained on the same protocol and followed it during the grading task. Although the agreement between them was in general good, Grader 2 had more tolerance than Grader 1. Grader 1 had considerable experience of grading colour fundus images in the context of various retinal diseases. It is possible that even with the protocol we used, this experience meant an ingrained preference for images with better overall quality.

iExaminer images benefited more from dilation, with this having relatively little effect on the proportion of D-Eye images graded as at least adequate. Because the quality grading we employed was specific to this study, caution should be exercised in making comparisons with other studies. However, Bastawrous et al.<sup>13</sup>, working with a large dataset obtained in Kenya (2920 eyes imaged), also compared smartphone and digital retinal camera optic disc images obtained from dilated eyes. While they provided little detail about the criteria used to judge image acceptability, they reported a higher proportion of unacceptable images obtained with the smartphone (13% vs 6%). Their overall much higher proportion of acceptable images compared with our study is almost certainly due to different criteria being used in the two studies.

For images graded as at least acceptable, inter-observer agreement for the CDR extracted from them was good with ICCs of 0.885 or better, no marked differences between devices, and no great improvement with dilation. Intra-observer agreement was also good (ICC = 0.909 or better) across devices and conditions. When data from images obtained with the two smartphone devices were compared to images obtained from dilated eyes with the reference camera for both graders, we observed poorer agreement represented by generally lower ICC's. CDR calculated from images obtained with the smartphone systems was systematically significantly lower than that calculated from the reference camera images; this was evidenced by negative mean differences, with confidence limits that did not straddle 0. However, overall these differences were small.

Russo et al.<sup>14</sup> compared the D-Eye to slit-lamp biomicroscopy for grading vertical CDR in the undilated eyes of 110 patients with either ocular hypertension or glaucoma. For the 107 eyes in which grading was possible, the difference between CDR measurements for the two techniques was not statistically significant. Judging from the example images provided (their Figure 1), the image quality was probably comparable between their study and ours (our Figure 4A). Their measurements of vertical CDR did not differ significantly between the two imaging approaches. While superficially this appears to contrast with our results, we explicitly compared image quality, whereas they compared grading performance. The explicit image grading criteria which we employed probably explains the difference between studies.

Assessing the overall image quality of the acquired images from the two smartphone-based devices, according to the UK National Screening Standards (UK National Screening Committee, Essential Elements in Developing a Diabetic Retinopathy Screening Programme (Workbook 4.3). 2009), the percentage of images with adequate or above quality was <25% for both the devices with and without dilation. This is well below the requirements for screening within a programme like the UK National Diabetic Eye Screening Programme, but are again because of the specific criteria we applied. However, Russo et al.<sup>5</sup> reported promising results in terms of accuracy and reliability of D-Eye to grade diabetic retinopathy (DR) in patients with diabetes mellitus. They compared D-Eye with slit-lamp biomicroscopy on 240 eyes from 120 outpatients. They graded images using a 5-step scale and found considerable agreement between biomicroscopy and D-Eye for the grading of DR. In their study the image quality was not graded. Overall the quality of the illustrative images shown appears to be inferior to the standard of screening practice. While this suggests that currently image quality would not allow smartphone based assessment in formal screening, there may be other settings where smartphone-based imaging would be useful.

Smartphones do have a number of advantages over traditional cameras that could be exploited to enhance the overall performance of the information a smartphone-based imaging system might provide. For the purposes of our experiment we manipulated the images offline. An effort was made to crop and resize images so as to reduce possible bias caused by the image aspect ratio and different retinal areas covered by different devices. However, advanced and optimised automated image analysis techniques could be run on the smartphones themselves, exploiting their burgeoning computing power. For instance, from a video or multiple images set, an image covering larger field of view with improved resolution might be achieved<sup>18</sup> and automatic cup and disc measurement tools might be added<sup>19</sup>. The inherent connectivity of smartphones could allow them to be integrated with electronic patient records or incorporated in patient management systems<sup>20</sup>.

Finally, our study did reveal a number of usability issues. It took 130.7s to acquire 20 multiple still images with the D-Eye, while iExaminer took 147.6s to acquire 9 multiple still images. Essentially it took a shorter time using D-Eye than iExaminer in order to take the same number of images. While both devices support video acquisition, we did not investigate the usability of videos and the images that might be extracted from them. A number of patients experienced seeing green or dark spots after the intense light from iExaminer. Some felt uncomfortable due to the D-Eye device touching their eye lashes during the image acquisition. However, the smaller, lighter and more compact D-Eye did appear to be easier to operate than the iExaminer design. As with any new technology, further optimisation of both devices and procedures will achieve improved results.

## Conclusion

The smartphone-based imaging systems we investigated both showed promise for imaging the optic disc of patients with diagnosed or suspected glaucoma, with the D-Eye slightly out-performing the iExaminer. In circumstances where a fundus camera is not available, these devices might have a role in recording the appearance of key ocular structures and aiding in the detection and management of disease.

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